REMARKS/ARGUMENTS

Upon entry of the present amendment, claims 380-423 are pending in the application. The amendment to claim 380 is made to correct a grammatical error; "inactive" is replaced with "inactivate". The amendment to claim 399 is made to correct an obvious typographical error; "eat Shock Protein" has been replaced with "Heat Shock Protein". No new matter is added by the present amendment.

The presently claimed invention is directed to, *inter alia*, methods for conjugating a peptide immunogen to a carrier protein by derivatizing functional groups on the carrier, reacting the carrier with the peptide immunogen to form a conjugate, and capping unreacted derivatized functional groups on the conjugate. The claimed invention also extends to the conjugates themselves, compositions comprising the conjugates, and methods for inducing an immune response via administration of the conjugates to a subject.

I. Lack Of Unity Rejection

A. Groups I-XC Share At Least One Special Technical Feature

The Examiner has restricted the claimed invention into ninety groups on the basis that the inventions are not so linked as to form a single general inventive concept under PCT Rule 13.1. The Examiner states that Groups I-XC do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. By way of example, the Examiner states that the technical feature of Group II is the conjugation of a peptide immunogen comprising Aβ via a reactive group of an amino acid residue to a derivatized carrier protein comprising keyhole limpet hemocyanin, which is allegedly shown by Shimizu *et al.*, *Journal of Neuroscience Research*, 70:451-461 (2002).

Applicants respectfully submit that the claims are linked to form a single general inventive concept under PCT Rule 13. PCT Rule 13.2 addresses the circumstances in which the requirement of unity of invention is to be considered fulfilled. The rule states that unity of invention is fulfilled "when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features." The expression "special

technical features" means those technical features that define a contribution over the prior art. Accordingly, unity is satisfied between two groups of claims if the groups have *a* special technical feature in common. The rule does not require that two groups of claims have every technical feature in common. Here, all of the claims recite, *inter alia*, a peptide immunogen comprising Aβ, or a fragment or analog thereof conjugated to a carrier protein via one or more derivatized functional groups, and the *capping of unreacted derivatized functional groups*. Claims 380 and 389 recite a method of conjugating a peptide immunogen to a carrier protein comprising, *inter alia*, reacting the conjugate with a capping reagent to inactivate unreacted functional groups on the carrier. Claims 398 and 404 recite a conjugate of a peptide immunogen to a carrier protein comprising, *inter alia*, a capping molecule covalently attached to a derivatized functional group of the carrier. Claim 410 recites a composition comprising a conjugate generated by the method of claim 389, discussed above, and claim 417 recites a method of inducing an immune response in a subject via administration of the composition of claim 410. All other claims in the application depend from these six claims. Thus, each of the presently pending claims includes capping a derivatized functional group on the carrier of the Aβ peptide immunogen-protein carrier conjugate.

The Shimizu reference cited by the Examiner discusses conjugation of an isomerized A-beta peptide to maleimide-activated KLH. *See* p. 452, 2nd column, last paragraph. Nowhere does Shimizu discuss capping derivatized functional groups of the conjugate, as recited in the presently claimed invention. Because at least this feature is not present in the art cited by the Examiner, it constitutes a special technical feature unifying all of the presently pending claims. Thus, the requirement for unity of invention is fulfilled with regard to all of the presently pending claims for at least the reasons discussed above.

B. Shimizu Does Not Show the Special Technical Feature of Group II

The Examiner has taken the position that the technical feature of Group II is shown by Shimizu. *See* paragraph bridging pp. 4-5 of the Office Action. Based on this discussion, the Examiner states that Group II (which corresponds to the KLH species of

protein/polypeptide carrier recited in claim 381) does not make a contribution over the prior art, and concludes that Groups I-XC therefore lack unity of invention.

As discussed above, the claims are unified, not by the species of protein/polypeptide carrier to which the peptide immunogen is conjugated, but by the recitation of capping derivatized functional groups on such conjugates. Thus, the allegedly distinct inventions identified by the Examiner are unified by at least this special technical feature.

II. Restriction Requirement

As discussed above, the Examiner has restricted the currently pending claims into 90 restriction groups. Groups I-XXX are drawn to a method of conjugating a peptide immunogen to a carrier protein. Groups XXXI-LX are drawn to a conjugate of a peptide immunogen with a carrier protein. Groups LXI-XC are drawn to a method of inducing an immune response via administration of a conjugate comprising a peptide immunogen and a carrier protein.

Applicants respectfully traverse the restriction requirement for the reasons discussed above, and submit that an election of species requirement, rather than a restriction requirement, is the appropriate action with respect to the species of protein/polypeptide carrier recited in dependent claims 381, 382, 390, 391, 399, 400, 405, 406, 411, 412, 418, and 419. Although it appears that the Examiner is effectively treating the restriction requirement between the various species of protein/polypeptide carrier as an election of species requirement as it pertains to each of Groups I-XXX, XXXI-LX, and LXI-XC, respectively (*see, e.g.*, p. 3, 1st full paragraph of the Office Action in which the Examiner qualifies the restriction requirement by non-allowance of the linking claims), applicants submit that this is improper given the unifying special technical feature discussed above. Thus, applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement, and instead require an election of species of a protein/polypeptide carrier.

A. Election of Restriction Group and Species

Subject to the traversal discussed herein, applicants elect Group XLV, directed to conjugates and immunogenic compositions comprising conjugates, in which the

protein/polypeptide carrier is CRM_{197}. Claims 398-416 encompass the elected invention. Claims 398-399, 401-405, 407-411 and 413-416 are generic to the elected species of protein/polypeptide carrier, and claims 400, 406 and 412 read on the elected species.

1. Aβ Peptide or Fragments or Analogs thereof

In response to the election of species requirement set forth at p. 6, 2nd paragraph under "Election of Species," applicants elect a peptide immunogen having the amino acid sequence of SEQ ID NO:2 (*i.e.*, DAEFRHD-C) as the species of Aβ peptide or fragments or analogs thereof. Elected claims 398-402, 404-408, 410-414 and 416 are generic to and encompass the elected species of Aβ peptide or fragments or analogs thereof. Claims 403, 409, and 415 read on the elected species.

2. Cross-linking Reagent

In response to the election of species requirement set forth at p. 6, 4th paragraph under "Election of Species," applicants elect N-Succinimidyl bromoacetate as the species of cross-linking reagent. Elected claims 398-416 are generic to and encompass the elected species of cross-linking reagent.

3. Capping Reagent

In response to the election of species requirement set forth at p. 7, 1st paragraph, applicants elect N-Acetylcysteamine as the species of capping reagent. Elected claims 398-416 are generic to and encompass the elected species of capping reagent.

4. Structurally-defined Conjugate

In response to the election of species requirement set forth at p. 7, 3rd paragraph, applicants elect a molecule wherein C is CRM_{197} having the amino acid sequence of SEQ ID NO:40, X is the amino functional group of a lysine residue, m is 39, X^d is the amino functional group of the lysine residues derivatized with N-Succinimidyl bromoacetate, P is a peptide immunogen having the amino acid sequence of SEQ ID NO:2 with a C-terminal cysteine residue, such that X^d-P yields (remainder of lysine residue)-NH-$C(O)CH_2$-S-(remainder of cysteine residue)-(remainder of peptide immunogen), n is 14, R is $SCH_2CH_2NHC(O)CH_3$ such that X^d-R yields (remainder of lysine residue)-NH-$C(O)CH_2$-$SCH_2CH_2NHC(O)CH_3$, p is 6, and

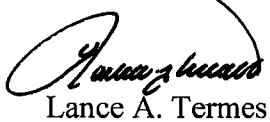
the derivatized lysine residues correspond to every other lysine residue of the CRM_{197} protein carrier beginning with the first N-terminal lysine residue: GADDVVDSS**K**. Claims 398-403 are generic to and encompass the elected species of structurally-defined conjugate.

B. Proposed Alternate Restriction Requirement

Alternatively, applicants propose that the Examiner could restrict the claims into 3 groups, defined by the current Groups I-XXX, XXXI-LX, and LXI-XC, respectively, and require an election of species regarding the protein/polypeptide carrier, as discussed above. This restriction requirement should be subject to rejoinder, as discussed at pp. 5-6 of the Office Action.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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